UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Registration of the End-Use Product, NEU 1161I [Canola Oil + Pyrethrins (File Symbol 67702-L)] containing the active ingredients, Canola Oil (PC Code 011332)and Pyrethrin Extract (PC Codes 069001 + 063501). Canola Oil + Pyrethrins contains 89.5% canola oil, 2.5% Pyrethrum Extract and 8% Inerts. Review of Product Chemistry Data MRID Nos. 440734-01 and 440769-02 and Toxicology Data MRID Nos. 440769-04, -05, 441577-01, 440769-06, 440769-07; Submission No. S518236; DP Barcode No. D233197.

FROM: Paul L. Zubkoff, Ph.D., Chemist Date: December 15, 1997 Paul L. Zubkoff
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511W)

Sheryl Reilly, Ph.D., Biologist Sheryl K Reilly 12-15-97
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511W)

TO: Susanne Cerrelli, Registration Action Leader
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511W)

ACTION REQUESTED:

Walter G. Talarek, on behalf of W. Neudorff GmbH KG, Emmerthal, Germany requests registration of an end-use product, Canola Oil + Pyrethrins, (File Symbol 67702-L) containing the active ingredients, Canola Oil and Pyrethrum Extract (20%) for control of egg stages of pests present in the dormant season and scale insects, mites and mealybugs on dormant shrubs, evergreens, woody plants, fruit trees and shade trees and numerous agricultural crops. Canola Oil + Pyrethrins is a biochemical control agent containing 89.5% canola oil, 2.5% Pyrethrum Extract and 8% inert ingredients.

CONCLUSIONS AND RECOMMENDATIONS:

1. The submitted product chemistry data for biochemical pest control agent, Canola Oil + Pyrethrins, satisfy the requirements for 40 CFR §158.690(a): 151-10 Product Identity; 151-11 Manufacturing Process; 151-12 Discussion of Formation of Unintentional Products; 151-13 Analysis of Samples; 151-15 Certification of Limits; 151-16 Analytical Methods; and 151-17 Physical and Chemical

Properties. These properties are listed in Table 1.

2. The submitted toxicity data for biochemical pest control agent, Canola Oil + Pyrethrins, satisfy the requirements for 40 CFR §158.690(c): 151-10 Acute Oral Toxicity; 152-11 Acute Dermal Toxicity; 152-12 Acute Inhalation Toxicity; 152-13 Primary Eye Irritation; and 152-14 Primary Dermal Irritation; 152-13 Hypersensitivity (Buehler) is satisfied by waiver. The Toxicology Category is III.

Guideline No.	Title	Species	Measurement	Toxicity Category
152-10	Acute Oral	Rat	LD_{50} > 2.0 g/kg	III
152-11	Acute Dermal	Rabbit	LD_{50} > 2.0 g/kg	III
152-12	Acute Inhalation	Rat	LC_{50} > 2.36 mg/L air	IV
152-13	Primary Eye Irritation	Rabbit	Primary Eye Irritation Index = 3.3	IV minimally irritating
152-14	Primary Dermal Irritation	Rabbit	Primary Irritation Index = 2.5	III moderately irritating
152-15	Hypersensitivity (Buehler)	Guinea Pig	Satisfied by Waiver	N/A

2. Based on the toxicity data for this end-use product and the knowledge that all inert ingredients used in this product are already cleared by the Agency for food-use, and an exemption from the requirement of a tolerance has been issued for the active ingredient, Pyrethrins under 40 CFR §180.128 in or on all raw agricultural commodities when applied as a pest control agent or post-harvest pest control agent in accordance with good agricultural practices (40 CFR 180.128), all requirements for toxicity testing are satisfied.

3. Summaries of the NEU 1161l Canola Oil + Pyrethrins acute toxicity studies follow.

152-10 Acute Oral Toxicity **Rat** **MRID No. 440769-04**

The oral LD_{50} of NEU 1161l in Wistar Rats is >2.0 g/kg body weight and the Toxicity Category is III.

152-11 Acute Dermal Toxicity **Rat** **MRID No. 440769-05**

The rat dermal LD_{50} of NEU 1161l (Canola Oil + Pyrethrins) on Wistar rats is >2000 mg/kg body weight and the Toxicity Category is III.

152-12 Acute Inhalation Toxicity **Rat** **MRID No. 441577-01**

The acute inhalation of NEU 1161l (Canola Oil + Pyrethrins) in Sprague-Dawley albino rats is greater than 2.36 mg/L air (the highest technically achievable concentration) over a 4 hour period of exposure for the inhalation route. The Toxicity Category is IV for NEU 1161l (Canola Oil + Pyrethrins).

No mortality occurred in the acute inhalation study of NEU 1161l (Canola Oil + Pyrethrins) at 2.36 mg/L air of the test substance (the highest technical achievable concentration) by the inhalation route during a single continuous period of 4 hours for rats. No acute toxicological symptoms were observed over a 14-day period of observation and no abnormal organs were observed during post-mortem examinations.

152-13 Primary Eye Irritation **Rabbit** **MRID No. 440769-06**

The acute eye irritation/corrosion study carried out with NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary eye irritation index of 3.3 (minimally irritating) [Kay & Calandra interpretation of the Draize score]. Instillation resulted in slight irritation of the conjunctival tissue, which had resolved within 24 hours. The Toxicity Category is IV (minimally irritating).

152-14 Primary Dermal Irritation **Rabbit** **MRID No. 440769-07**

The primary skin irritation/corrosion study carried out with the end-use product NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary irritation index of 2.5 when applied to the intact skin (moderately irritating). The Toxicity Category is III (moderately irritating).

152-15 Hypersensitivity (Buehler) **Guinea Pig** **MRID No. 440769-00**

A waiver for an exemption from the requirement to generate data has been submitted based on the acute dermal and primary dermal studies (both Toxicity III) submitted with this registration application. Based on the proposed use patterns proposed on the label, no significant exposure from repeated skin contact is expected. However, if incidents do occur during usage, the Registrant must submit incident reports. The waiver from the requirement to generate data is granted.

cc: S. Cerrelli, P. Zubkoff, BPPD Subject File
P. Zubkoff (703) 308-8694
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Table 1: Summary of NEU 1161l Canola Oil + Pyrethrins File Symbol 67702- L

Guideline	Study	Result		MRID #
151-B-10	Product Identity	A	See CBI Appendix	440769-01
151-B-11	Manufacturing Process	A	See CBI Appendix	440769-01
151-B-12	Discussion of formation of unintentional ingredients	A	See CBI Appendix	440769-01
151-B-13	Preliminary Analysis	A	See CBI Appendix	440769-02
151-B-15	Certification of limits	A	See CBI Appendix	440769-02
151-B-16	Analytical methods	A	See CBI Appendix	440769-02
151-17	**Physical/Chemical Properties**			
a	color	A	Yellow	440769-03
b	physical state	A	Clear liquid, no inclusions	440769-03
	odor	A	Typical pyrethrin odor	440769-03
d	melting point	N/A	Technical material is liquid	Administrative
e	boiling point	N/A	a.i. is mixture of naturally occurring substances	Administrative
f	density	A	0.9204 ±0.0005 g/ml @ 20.0°C	440769-03
g	solubility	A	Technical is insoluble in water & ethanol; soluble in mineral oil; end product is dispersible in water	Administrative
	vapor pressure		Product specific waiver requested a.i. of product < 0.1 mm Hg @ 19.5°C#	
	dissociation constant	N/A	Waiver granted	Administrative
	octanol/water partition coefficient	N/A	Toxicology studies do not indicate need for information	Administrative
l	pH 1% solution	A	6.63±0.11	440769-03
	stability	A	table#	440555-06#
	oxidizing or reducing	N/A	Waiver granted	Administrative
k	flammability / flash pt.	N/A	315°C (Cleveland Open Cup Method)# product contains no combustible fluids	
	explodability	N/A	Waiver granted	Administrative
	storage stability	A	Canola oil shows no change @ 54°C for 1 month Pyrethrins show no change @ 54°C for 1 month	440769-03* 440769-03
	viscosity	A	67.1±0.01 centipoise (Brookfield viscometer/#1)	440769-03*
n	miscibility	N/A	Product specific waiver requested / product is not to be diluted with hydrocarbons	Administrative

Guideline	Study	Result	MRID #
	corrosion characteristics	Aluminum 0.220 (mpy) No visible change Brass 0.387 (mpy) No visible change Galvanized 1.684 (mpy) No visible change Stainless Steel 0.342 (mpy) Surface slightly dulled Zinc 0.402 (mpy) No visible change Copper 0 .040 (mpy) Slight darkening of pipe in patches	440769-03*
	dielectric breakdown voltage	N/A Not used near electrical controls or devices	

A = Acceptable N/A = Not Applicable Physical/Chemical Properties: * G.L.P. Study # G.L..P. Unknown

Table 2. NEU 1161l Canola Oil + Pyrethrins File Symbol 67702- L

Chemistry	Abbreviated Title	Status	Rationale for Waiver	MRID
CSF	Ingredients	Acceptable		
Label	Label			
151-10	Product Identity	Acceptable		440769-01
151-11	Manufacturing Process	Acceptable		440769-01
151-12	Unintentional Ingredients	Acceptable		440769-01
151-13	5 Analyses	Acceptable		440769-02
151-15	Analytical Methods	Acceptable		440769-02
151-16	Certification of Limits	Acceptable		440769-02
151-17	Properties	Acceptable		440769-03
Toxicology				
Tolerance	Tolerance Petition			6F4747
152-10	Acute Oral (rat)	Acceptable	LD_{50} > 2000 mg/kg Toxicity III	440769-04
152-11	Acute Dermal (rat)	Acceptable	LD_{50} > 2000 mg/kg Toxicity III	440769-05
152-12	Acute Inhalation (rat)	Acceptable	LD_{50} > 2.36 mg/L air Toxicity IV	441577-01
152-13	Primary Eye (rabbit)	Acceptable	Draize = 3.3 Toxicity IV Minimally Irritating	440769-06
152-14	Primary Dermal (rabbit)	Acceptable	Primary Irritatn Index = 2.5 Moderately Irritating Toxicity III	440769-07
152-15	Hypersensitivity	Waiver Granted	8,9 Soybean Oil	Administrative
152-16	Hypersensitivity Incidents	Waiver Granted	4 no known incidents	Administrative
152-17	Genotoxicity	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
152-18	Immune Response	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
152-20	90 Day Feeding	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
152-21	90 Day Dermal	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
152-22	90 Day Inhalation	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
152-23	Teratogenicity	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
Ecotoxicity				
154-6	Avian Acute Oral	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
144-7	Avian Acute Diet	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
154-8	Freshwater Fish	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
154-9	Freshwater Invert	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
154-10	Non-Target Plant	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative
154-11	Bee	Waiver Granted	1, 2, 3, 4, 5, 6, 7	Administrative

1 Known low toxicity and risks of canola oil
2 Known natural occurrence and abundance of canola oil
3 Widespread use of canola oil as edible fats and oils
4 FDA GRAS status of canola oil as an edible fat or oil in human food 21 CFR §184.1555(c)
5 Non-toxic mode of action of canola oil
6 Anticipated low volume use in pesticide products of canola oil
7 Data are available in the open literature for canola oil
8 Reregistration Eligibility Decision (RED): Flower and Vegetable Oils EPA 738-R-93-031 December 1993
9 Anticipated low exposure from proposed use patterns
10 Pyretrhrin component is eligible for formulator's exemption provided that labeling is comensurate with other pyrethrin products

DATA EVALUATION RECORD

REVIEWED BY:	Paul L. Zubkoff, Ph.D. Chemist, BPPD (7511W)	Signature: Date:	Paul L Zubkoff October 15, 1997
PEER REVIEWED BY:	Sheryl Reilly, Ph.D. Biologist, BPPD (7511W)	Signature: Date:	Sheryl K Reilly 10-16-97

STUDY TYPE: Toxicology - End-Use Product
GUIDELINE: 152-10 Toxicology: Acute Oral Toxicity

MRID NO.: 440769-05
EPA ID NO.: 67702-L
PC CODE: 011332

DP BARCODE: D233197
CASE NO.: 060560
SUBMISSION: S518236

OBJECTIVE: Registration / New Biochemical / Food/Feed Use
TEST MATERIAL: NEU1161I
SYNONYMS: Canola Oil + Pyrethrins
Canola Oil (011332) + Pyrethrins (069001 + 065301)

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, Postfach 1209, D-31860 Emmerthal, Germany

TESTING FACILITY: NOTOX, Hambakenwetering 3, 5203 DL's-Hertogenbosch, Netherlands, P.O. Box 3476

TITLE OF REPORT: **NEU1161I End-Use Product: Canola Oil + Pyrethrins**
Vol 5. Toxicology Data: Acute Oral Toxicity Study

40 CFR 158.690; Guideline 152-10 **MRID No. 440769-04**

AUTHOR: W. R. Pels Rijcken

REPORT ISSUED: May 15, 1996 EPA Date: August 5, 1996

CONCLUSION:

The rat oral LD_{50} of NEU 1161I is >2000 mg/kg body weight and the Toxicity Category is III. This submission satisfies data requirements for 152-10.

EXECUTIVE SUMMARY:

152-11 Acute Toxicity (Rat) NEU1161I Canola Oil + Pyrethrins

The rat oral LD_{50} of NEU 1161I is >2000 mg/kg body weight and Toxicity Category is III. This study satisfies data requirement, 152-10.

Methods:

Five rats of each sex were administered 2000 mg/kg of NEU 1161I by oral gavage. Daily observations were made and body weights were determined weekly. After terminal sacrifice (day 15), macroscopic examinations were made.

Group housing of 5 animals per sex in polycarbonate cages in an air conditioned room with ~15 air changes per hour,

21°C, 50% relative humidity and artificial light with 12 h on and 12 h off. Animals were acclimated for 5 days and fed a standard laboratory pellet diet (Carfil Quality BVBA, Oud-Turnhout, Belgium) with free access to tap-water. Before dosing, food was witheld overnight and until 3-4 hours after dosing.

Procedures:

The test substance, NEU 1161I (2000 mg/g body weight), was adminstered by stainless steel stomach tube as a single dose. Viability and mortality were checked twice daily for 14 days; animals were checked for clinical signs periodically on the first day, and daily thereafter until day 15. At end of observation period, animals were sacrified by O_2 /CO_2 asphyxiation and subjected to necropsy. Descriptions of internal macroscopic abnormalities were noted.

Test Materia:l

Identification	NEU 1161I	90% Canola Oil, 2% pyrethum
Batch	2/96	
Purity	90% Rapeseed Oil 2% Pyrethrum	
Expiration Date	February 12, 2001	
Specific Gravity	0.917	
Preparation	*Test material was administered by a single undiluted dose as obtained from sponsor at* 2000 mg/kg body weight	

Test Species and Source

Rat, Wistar strain Crl: (WI) BR (outbred, SPF Quality). Recognized by international guidelines. Source: Charles River, Sulzfeld, Germany

Age: ~6 weeks	Body Weight:	Within ± 20% of the sex mean
No of animals:	5 male, 5 female	

Observations:

No mortalities occurred during the tests and there were no clinical signs of toxicity. Body weight gains were considered normal for rats undergoing these studies. No abnormalities were found upon macroscopic examination post mortem.

Body Weights:	5 ♂:	day	1	8	15
		(g)	190	266	317
		Std. Dev.	14	15	12
	5♀:	(g)	155	198	224
		Std. Dev.	6	15	18

Conclusion:

The rat oral LD_{50} of NEU 1161I (Canola Oil + Pyrethrins) is >2000 mg/kg body weight, Toxicity Category III. This study satisfies the data requirement, 152-10.

CONFIDENTIALITY AND GOOD LABORATORY PRACTICES STATEMENTS

A signed statement of no confidentiality is made for the information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1) (A), (B), or (C).

A signed statement indicates that this study has been conducted in compliance with OECD "Principles of Good Laboratory Practice (essentially in conformity with 40 CFR Part 160, "Good Laboratory Practices").

cc: S. Reilly, P. Zubkoff, BPPD Subject File
P. Zubkoff: (703) 308-8694 10/15/97
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DATA EVALUATION RECORD

REVIEWED BY:	Paul L. Zubkoff, Ph.D. Chemist, BPPD (7511W)	Signature: Date:	Paul L. Zubkoff October 15, 1997
PEER REVIEWED BY:	Sheryl Reilly, Ph.D. Biologist, BPPD (7511W)	Signature: Date:	Sheryl K Reilly 10-16-97

STUDY TYPE:	**Toxicology - End-Use Product**
GUIDELINE:	**151-11 Toxicology: Acute Dermal Toxicity**
MRID NO.:	440769-05
EPA ID NO.:	67702-L
PC CODE:	011332
DP BARCODE:	D233197
CASE NO.:	060560
SUBMISSION:	S518236
OBJECTIVE:	Registration / New Biochemical / Food/Feed Use
TEST MATERIAL:	NEU1161I
SYNONYMS:	Canola Oil + Pyrethrins Canola Oil (011332) + Pyrethrins (069001 + 063501)
SPONSOR:	W. Neudorff GmbH KG, An der Mühle 3, Postfach 1209, D-31860 Emmerthal, Germany
TESTING FACILITY:	NOTOX, Hambakenwetering 3, 5203 DL's-Hertogenbosch, Netherlands, P.O. Box 3476

TITLE OF REPORT:	**NEU1161I End-Use Product:** **Vol 6. Toxicology Data: Acute Dermal Toxicity Study** **40 CFR 158.690; Guideline 152-11** **MRID 440769-05**
AUTHOR:	W. R. Pels Rijcken
REPORT ISSUED:	May 15, 1996 EPA Date: August 5, 1996

CONCLUSION:

The dermal LD_{50} of NEU 1161I (Canola Oil + Pyrethrins) is >2000 mg/kg body weight and the Toxicity Category is III. Although only 3 animals were used in this test, the quantitative result places this end-use product in Toxicity Category III. This submission satisfies data requirements for 152-11.

EXECUTIVE SUMMARY:

152-11 Acute Dermal Toxicity (Rat) NEU1161I Canola Oil + Pyrethrins

The rat dermal LD_{50} of NEU 1161I (Canola Oil + Pyrethrins) is >2000 mg/kg body weight and the Toxicity Category is III. This study satisfies the data requirement for 152-11.

Methods:

Five rats of each sex were subjected to 2000 mg/kg of NEU 1161I by dermal application for 24 hours. Hair from backs of animals was clipped (♂: 25 cm^2, ♀: 18 cm^2) one day before application of test substance; NEU 1161I (2000 mg/g body weight) test material was applied as single dose. The application area was covered; viability and mortality was checked twice daily; animals were checked for clinical signs periodically on the first day , and daily thereafter. Time of onset and duration were noted. Observations for body weights were made weekly. At the end of the observation period, animals were sacrificed by O_2/CO_2 asphyxiation and subjected to necropsy. Descriptions of internal macroscopic abnormalities were noted. After terminal sacrifice, macroscopic examinations were made.

Animals were held individually in polycarbonate cages in an air conditioned room with ~15 air changes per hour, 21°C, 50% relative humidity and artificial light with 12 h on and 12 h off, fed laboratory pellet diet (Carfil Quality BVBA, Oud-Turnhout, Belgium) with free access to tap-water.

Test Material:

Identification	NEU 1161I	90% Canola Oil, 2% Pyrethrum
Batch	2/96	
Purity	90% Rapeseed Oil 2% Pyrethrum Extract	
Expiration Date	February 12, 2001	
Specific Gravity	0.917	
Preparation	Test material was applied undiluted as obtained from sponsor at 2000 mg/kg body weight	

Test Species and Source

Rat, Wistar strain Crl: (WI) BE (outbred, SPF Quality). Recognized by international guidelines. Source: Charles River, Sulzfeld, Germany

Age: ~8 weeks	Body Weight:	Within ± 20% of the sex mean
No of animals:	5 male, 5 female	

Observations:

No mortalities occurred during the tests. Body weight gains were within the range expected for rats undergoing these studies. No abnormalities were found upon macroscopic examination post mortem.

Clinical Signs: Red staining on head or neck of 1 ♀ from day 2 onward.

Body Weights:

		Day	1	8	15
5 ♂:	(g)		317	341	382
	Std. Dev.	11	25	34	
5♀:	(g)		208	215	220
	Std. Dev.	11	11	12	

Statistics: No statistical analysis.

Conclusion:

The rat dermal LD_{50} of NEU 1161I (Canola Oil + Pyrethrins) in rats is > 2000 mg/kg body weight, Toxicity Category III.

CONFIDENTIALITY AND GOOD LABORATORY PRACTICES STATEMENTS

A signed statement of no confidentiality is made for the information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1) (A), (B), or (C).

A signed statement indicates that this study has been conducted in compliance with OECD "Principles of Good Laboratory Practice (essentially in conformity with 40 CFR Part 160, "Good Laboratory Practices").

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DATA EVALUATION RECORD

REVIEWED BY:	Paul L. Zubkoff, Ph.D. Chemist, BPPD (7511W)	Signature: Date:	Paul L. Zubkoff October 15, 1997
PEER REVIEWED BY:	Sheryl Reilly, Ph.D. Biologist, BPPD (7511W)	Signature: Date:	Sheryl K Reilly 10-16-97

STUDY TYPE: Toxicology - End-Use Product
GUIDELINE: 151-12 Toxicology: Acute Inhalation Toxicity

MRID NO.: 441577-01
EPA ID NO.: 67702-L
PC CODE: 011332

DP BARCODE: D233197
CASE NO.: 060560
SUBMISSION: S518236

OBJECTIVE: Registration / New Biochemical / Food/Feed Use
TEST MATERIAL: NEU1161I
SYNONYMS: Canola Oil + Pyrethrins
Canola Oil (011332) + Pyrethrins (069001)

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, Postfach 1209, D-31860 Emmerthal, Germany

TESTING FACILITY: BioChem GmbH, D-76185 Karlsruhe, Daimlerstraße 5 b, Germany

TITLE OF REPORT: **NEU1161I End-Use Product:**
Vol 7. Toxicology Data: Acute Inhalation Toxicity Study

40 CFR 158.690; Guideline 152-12 **MRID 441577-01**

AUTHOR: Dr. G. Lenz

REPORT ISSUED: April 16, 1996 EPA Date: August 5, 1996

EXECUTIVE SUMMARY:

152-12 Acute Inhalation Toxicity (Rat) NEU1161I (Vegetable Oil Spray) + Pyrethrins

The rat acute inhalation of NEU 1161I (Canola Oil + Pyrethrins) is greater than 2.36 mg/L air (the highest technically achievable concentration) over a 4 hour period of exposure for the inhalation route. The Toxicity Category is IV for NEU 1161I (Canola Oil + Pyrethrins). This submission satisfies data requirements for 152-12.

CONCLUSION:

No mortality occurred in the acute inhalation study of NEU 1161I (Canola Oil + Pyrethrins) at 2.36 mg/L air of the test substance (the highest technical achievable concentration) by the inhalation route during a single continuous period of 4 hours for rats. No acute toxicological symptoms were observed over a 14-day period of observation and no abnormal organs were observed during

post-mortem examinations. The Toxicity Category for NEU 1161I (Canola Oil + Pyrethrins) is IV. This submission satisfies data requirements for 152-12.

Methods:

Five rats of each sex were subjected to 2.36 mg/L of NEU 1161I (nominal concentration of 5.0 mg/L) by acute inhalation for 4 hours. Observations were made for clinical signs daily and weights were obtained weekly. On day 15, the animals were sacrificed and autopsied for organ abnormalities.

INHALATION EXPOSURE UNIT

The exposure apparatus was a stainless steel inhalation assembly (SIT 3000 Föhr, Germany) fitted with a metal base, movable stainless steel drum closed at one end with openings for animal cages, exhaust air and analytical equipment and a wide glass tube for observation. The top was a metal plate with an assembled aerosol- generating nozzle. Transparent Makrolon restraint cages allowed animal nose and head exposure to the aerosol.

The aerosol-generating nozzle had quick mount inlets for pressurized air and formulation. The compressor assembly used a pressurized air supply for dry, dust-free and oil-free air. Pressure regulators with rotameter flow meters were used for controlling inlet, outlet and sampling flow. Other apparatus included pumps for exhaust air and aerosol sampling, gas meter for calibration of gas flows, temperature and humidity measuring unit connected to an xy recorder. An API Aerosizer® particle size analyzer mach 2 with 3 VKL 10 (Palas®) diluting stages was used. The entire unit was placed in a closed cabinet equipped with an exhaust air system.

Animals were held individually in polycarbonate cages in an air conditioned room with ~15 air changes per hour, 21±2°C, 50% relative humidity, artificial light with 12 h on and 12 h off, and fed laboratory pellet diet (Carfil Quality BVBA, Oud-Turnhout, Belgium) with free access to tap-water.

Test Material

Identification	NEU 1161I	90% Canola Oil, 2% Pyrethrum
Receipt No.	119 979/1/001	
Date	February 19, 1966	
Batch	2/96	
Purity	90% Rapeseed Oil 2% Natural Pyrethrum Surfactants	
Expiration Date	February 12, 2001	
Specific Gravity	0.916	
Preparation	Test material was applied as obtained from sponsor at 2.36 mg/L air but with addition of particle size stabilizer (polyethylene glycol)	

Test Species, Source and Husbandry

Albino Rat	Sprague-Dawley
Source	Harlan Winkelmann BmbH Gartenstraβe 27, D-33178 Borchen
ID No.	030-034 (female) 035-=039 (male)
Age	Not Given
Veterinary Prelim	Without morbid signs; females were nulliparous and non-pregnant
Diet	Haltungsdiät "ALMA 0801 H 1003", 8 g twice daily
Caging	Individually in commercial Makrolon cages with bedding; grate at top
Temperature	19-23°C
Relative Humidity	30-70%
Diurnal Period	12 h: 12 h

Acclimation period of 5 days, followed by exposure period (4 h) and 14 days of observations; sacrificed on day 15

Observations:

No mortalities occurred during the tests. Body weight gains were within the range expected for rats undergoing these studies. One ♀ rat showed slight symptoms of hunched posture on day 6 and one ♀ showed severe symptoms of apathy on day 7. No organ abnormalities were found upon macroscopic examination post mortem.

Clinical Signs: None

Body Weights:

		Day	0	1	8	14
5 ♂:	(g)		188.8	204.0	223.4	232.0
	ση		4.2	2.3	3.9	6.3
5♀:	(g)		185.8	189.0	201.6	206.2
	ση		5.6	2.7	3.8	3.5

Aerosol: The inhalation chamber ((31 cm diameter x 87 cm height) was saturated with NEU 1161I using nominal 50 mg / 5 mg expected test formulation per liter for a test of 4 hours. To 225 g of formulation (NEU1161I), 1.02 g of poly(ethylene glycol) PEG 400 was added for generating a flow of 15 L of aerosol per hour. (The PEG 400 was added to stabilize the aerosol particle distribution within the required range. The concentration, particle size distribution, particle number, relative humidity and temperature were measured in the test atmosphere during the test at the animals snout. Two test atmosphere samples were collected during exposure using a wash bottle with an upper layer of hexane. After collection, samples were analyzed by gas-liquid chromatography (GLC).

Particle sizes were determined with an API Aerosizer® mach 2 combined with 3 1:10 Palas® VKL 10 diluting stages. The particle sizes ranged between 0.10 and 200 µm (lower and upper mean particle size classes, respectively) with flow through at 5.01 L/min. The mean velocity of the measured particles was 4.2 m/s. Temperature, relative humidity and oxygen were measured in the chamber. Oxygen content of the chamber was the same as the ambient concentration. Airflow was adjusted and monitored from the air supply by calibrated rotameters.

Particle size distributions by aerodynamic diameter were presented as number distribution (mean 1.076 µ; 90% range from 0.6942 to 1.991 µ), volume distribution (mean of 1.647 µm; 90% range from 0.8697 to 3.568 µm) and by density (consistent with 0.92 g/ml).

Canola Oil: During exposure, 2 samples were obtained: 1st sample was 15 minutes duration; 2nd sample was 30 minutes duration. Airflow was 2.5 L/m resulting in 37.5 and 75.0 L of air passing through the wash bottles. After flow was stopped, trapped samples were transferred to flasks for extraction. Adsorption in water was followed by extraction, derivitization and quantitation by gas-liquid chromatography with determination made from primary peak; for GLC, margaric acid (hepadecanoic acid) served as internal standard. The rationale describing the heterogeneous dispersion (condensation) of the fatty acid in the aerosol chamber is acceptable.

The measurement of canola oil fatty acid in the aerosol from the 30 minute sample was 2.36 mg/L.

Statistics: No statistical analys was employed. The 90% ranges of aerosol particles were measured.

CONCLUSION:

No mortality occurred in the acute inhalation study of NEU 1161I (Canola Oil + Pyrethrins) at 2.36 mg/L air of the test substance (the highest technically achievable concentration) by the inhalation route during a single continuous period of 4 hours for rats. No acute toxicological symptoms were observed over a 14-day period of observation and no post-mortem observations of abnormal organs were made. The Toxicity Category is IV for NEU 1161I. This submission satisfies data requirements for 152-12.

CONFIDENTIALITY AND GOOD LABORATORY PRACTICES STATEMENTS

A signed statement of no confidentiality is made for the information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1) (A), (B), or (C).

A signed statement indicates that this study has been conducted in compliance with OECD "Principles of Good Laboratory Practice (essentially in conformity with 40 CFR Part 160, "Good Laboratory Practices").

cc: S. Reilly, P. Zubkoff, BPPD Subject File
P. Zubkoff: (703) 308-8694 10/15/97
c:\97wp\97canola\can_inhl.x15

DATA EVALUATION RECORD

REVIEWED BY:	Paul L. Zubkoff, Ph.D. Chemist, BPPD (7511W)	Signature: Date:	Paul L. Zubkoff October 15, 1997
PEER REVIEWED BY:	Sheryl Reilly, Ph.D. Biologist, BPPD (7511W)	Signature: Date:	Sheryl K Reilly 10-16-97

STUDY TYPE: **Toxicology - End-Use Product**
GUIDELINE: **152-13 Toxicology: Primary Eye Irritation**

MRID NO.: 440769-06
EPA ID NO.: 67702-L
PC CODE: 011332

DP BARCODE: D233197
CASE NO.: 060560
SUBMISSION: S518236

OBJECTIVE: Registration / New Biochemical / Food/Feed Use
TEST MATERIAL: NEU1161I
SYNONYMS: Canola Oil + Pyrethrins
Canola Oil (011332) + Pyrethrins (069001 + 063501)

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, Postfach 1209, D-31860 Emmerthal, Germany

TESTING FACILITY: NOTOX, Hambakenwetering 3, P.O. Box 3476, 5203 DL's-Hertogenbosch, Netherlands

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TITLE OF REPORT: **NEU1161I End-Use Product:**
Vol 9. Toxicology Data: Primary Eye Irritation

40 CFR 158.690; Guideline 152-13 **MRID 440769-06**

AUTHOR: W. R. Pels Rijcken

REPORT ISSUED: May 22, 1996 EPA Date: August 5, 1996

CONCLUSION:

The acute eye irritation/corrosion study carried out with NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary eye irritation index of 3.3 (minimally irritating) [Kay & Calandra interpretation of the Draize score]. Instillation resulted in slight irritation of the conjunctival tissue, which had resolved within 24 hours. The Toxicity Category is IV (minimally irritating). This submission satisfies the data requirements for 152-13.

EXECUTIVE SUMMARY:

The acute eye irritation/corrosion study carried out with NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary eye irritation index of 3.3 (minimally irritating) [Kay & Calandra interpretation of the Draize score]. Single samples of 0.1 ml of NEU 1161I (Canola Oil + Pyrethrins) were instilled into one eye of each of three rabbits. Observations were made at 1, 24, 48 and 72 hours after instillation. Instillation resulted in slight irritation of the conjunctival tissue,

which had resolved within 24 hours. The Toxicity Category is IV (minimally irritating). This submission satisfies the data requirements for 152-13.

Methods

After a health inspection prior to the test to ascertain that the animals are in a good state of health, three male rabbits were subjected to instilling 0.1 ml of NEU 1161I (~90 mg of NEU 1161I) into the conjuncival sac of one eye of each animal. The lower eye lid was gently pulled away from the eyeball. The lids were than held together for ~1 second to prevent loss of the test material. The other eye served as a reference control. Immediately after the 24 hour observation, a solution of 2% fluorescein in water (adjusted to pH 7.0) was instilled into both eyes of each animal to quantitatively determine corneal epithelial damage. Any bright green stained area, indicating epithelial damage, was estimated as a percentage of the total corneal area. The eyes of each animal were examined approximately 1, 24, 48 and 72 hours after instillation of the test substance. Irritation scores and a description of all other (local) effects were recorded and scored according to Draize et al (1944) and Kay & Calandra (1962). Parameters scored included corneal irritation (opacity, area of cornea), iris and conjunctival irritation (redness, chemosis, discharge).

Test Material

Identification	NEU 1161I	90% Canola Oil, 2% Pyrethrum
Batch	2/96	
Purity	90% Rapeseed Oil 2% Pyrethrum	
Storage	Room temperature in the dark	
Expiration Date	February 12, 2001	
Specific Gravity	0.917	
Preparation	Test material was applied undiluted as obtained from sponsor	

Test Species and Source

Albino Rabbit, New Zealand White, (SPF Quality). Source: Broekman Institute, Someren, The Netherlands

Age: ~7 weeks	Body Weight:	1207 - 1356 grams
No of animals:	3 male	

Conditions

Animals individually housed in cages with perforated floors, equipped with automatic drinking system and acclimated for 5 days in an air-conditioned room with ~15 air changes per hour and environment controlled for optimal conditions (21°C and 50% relative humidity) and fluorescent lighting (12 h on /12 h off). Diet was standard laboratory rabbit diet (LLK-20, pellet diameter 4 mm, Hope Farms, Woerden, The Netherlands), ~100 g per day.

Observations

Instillation of 0.1 ml of NEU 1161I into one eye of each of three rabbits resulted in slight irritation of the conjunctival tissue. **Irritation:** The irritation consisted of redness and/or chemosis and had resolved within 24 hours. No iridic irritation or corneal opacity were observed and treatment of the eyes with 2% fluorescein 24 hours after test substance instillation revealed no corneal epithelial damage in any of the animals. **Coloration:** No staining of peri-ocular tissues by the test material was observed. **Toxicity Symptoms / Mortality:** No symptoms of systemic toxicity were observed in the animals during the test period and no mortality occurred.

Clinical Signs:	Corneal Opacity		Iris	Conjunctivae		Discharge
	Opacity	Area		Redness	Chemosis	
1 hr	0	0	0	1abc	1a	0
	0	0	0	1ac	0	0
	0	0	0	1abc	1a	0
24 hr	0	0	0	0	0	0
	0	0	0	0	0	0
	0	0	0	0	0	0
48 hr	0	0	0	0	0	0
	0	0	0	0	0	0
	0	0	0	0	0	0
72 hr	0	0	0	0	0	0
	0	0	0	0	0	0
	0	0	0	0	0	0
		a = eyelids		b = nictitating membrane		c = sclera

Kay & Clanadra Interpretation of Draize Score = 3.3

Statistics: No statistical analysis.

Conclusion

The acute eye irritation/corrosion study carried out with NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary eye irritation index of 3.3 (minimally irritating) [Kay & Calandra interpretation of the Draize score]. Single samples of 0.1 ml of NEU 1161I (Canola Oil + Pyrethrins) were instilled into one eye of each of three rabbits. Observations were made at 1, 24, 48 and 72 hours after instillation. Instillation resulted in slight irritation of the conjunctival tissue, which had resolved within 24 hours. The Toxicity Category is IV (minimally irritating). This submission satisfies the data requirements for 152-13.

CONFIDENTIALITY AND GOOD LABORATORY PRACTICES STATEMENTS

A signed statement of no data confidentiality claims is made for the information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1) (A), (B), or (C).

A signed statement indicates that this study has been conducted in compliance with OECD "Principles of Good Laboratory Practice (essentially in conformity with 40 CFR Part 160, "Good Laboratory Practices").

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DATA EVALUATION RECORD

REVIEWED BY:	Paul L. Zubkoff, Ph.D. Chemist, BPPD (7511W)	Signature: Date:	Paul L. Zubkoff October 15, 1997
PEER REVIEWED BY:	Sheryl Reilly, Ph.D. Biologist, BPPD (7511W)	Signature: Date:	Sheryl Reilly 10-16-97

STUDY TYPE: Toxicology - End-Use Product
GUIDELINE: 152-14 Toxicology: Primary Dermal Irritation

MRID NO.: 440769-07
EPA ID NO.: 67702-L
PC CODE: 011332

DP BARCODE: D233197
CASE NO.: 060560
SUBMISSION: S518236

OBJECTIVE: Registration / New Biochemical / Food/Feed Use
TEST MATERIAL: NEU1161I
SYNONYMS: Canola Oil + Pyrethrins
Canola Oil (011332) + Pyrethrins (069001)

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, Postfach 1209, D-31860 Emmerthal, Germany

TESTING FACILITY: NOTOX, Hambakenwetering 3, 5203 DL's-Hertogenbosch, Netherlands, P.O. Box 3476

TITLE OF REPORT: NEU1161I End-Use Product:
Vol 9. Toxicology Data: Primary Dermal Irritation

40 CFR 158.690; Guideline 152-14 MRID 440769-07

AUTHOR: W. R. Pels Rijcken

REPORT ISSUED: May 22, 1996 EPA Date: August 5, 1996

CONCLUSION:

The primary skin irritation/corrosion study carried out with the end-use product NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary irritation index of 2.5 (moderately irritating). The Toxicity Category is III (moderately irritating). This submission satisfies the data requirements for 152-14.

EXECUTIVE SUMMARY:

Three rabbits were exposed to 0.5 ml of NEU 1161I applied to clipped skin for 4 hours using a semi-occlusive dressing. Observations were made at 1, 24 48, 72 hours and 7 days after exposure. Exposure to NEU 1161I resulted in defined erythema and slight edema in the treated skin areas of each animal. The skin irritation was resolved within 7 days in all three rabbits. The dermal application of NEU 1161I resulted in a primary irritation index of 2.5 (moderately irritating) when applied to the intact rabbit skin.

Methods

Three male rabbits were subjected to 0.5 ml of NEU 1161I (~500 mg of NEU 1161I) by dermal application to one flank with a surgical gauze patch (2x3 cm) for 4 hours. The patch was mounted with Micropore tape (3 M Co.) which was wrapped around the abdomen and secured with an elastic bandage. Four hours after application, the dressing was removed and test material removed by washing with tap water. Hair from the flanks of animals had been clipped one day before application of test substance as single dose. The application area was covered; viability and mortality was checked twice daily; animals were checked for clinical signs 1 hour, 24, 48 and 72 hours and 7 days after removal of the test materials and dressings. Adjacent areas served as controls. Scoring of erythema / eschar and oedema (irritation) was according to Draize.

Test Material

Identification	NEU 1161I	90% Canola Oil, 2% Pyrethrum
Batch	2/96	
Purity	90% Rapeseed Oil 2% Pyrethrum	
Storage	Room temperature in the dark	
Expiration Date	February 12, 2001	
Specific Gravity	0.917	
Preparation	Test material was applied undiluted as obtained from sponsor	

Test Species and Source

Albino Rabbit, New Zealand White, (SPF Quality). Source: Broekman Institute, Someren, The Netherlands

Age: ~8 weeks	Body Weight:	1410 - 1867 grams
No of animals:	3 male	

Conditions

Animals individually housed in cages with perforated floors, equipped with automatic drinking system and acclimated for 5 days in an air-conditioned room with ~15 air changes per hour and environment controlled for optimal conditions (21°C and 50% relative humidity) and fluorescent lighting (12 h on /12 h off). Diet was standard laboratory rabbit diet (LLK-20, pellet diameter 4 mm, Hope Farms, Woerden, The Netherlands), ~100 g per day.

Observations

Four hours of exposure to 0.5 ml of NEU 1161I resulted in well-defined erythema and slight edema in the treated skin areas in all animals. The skin irritation was completely resolved within 7 days in all animals. No staining of treated skin by the test substance was observed nor were symptoms of systemic toxicity observed during the test period and no mortality occurred.

Clinical Signs:	Erythema	Edema	Comments	
1 hr	2 2 2	2 2 2	–	
24 hr	2 2 2	1 1 1	–	
48 hr	2 2 2	0 0 0	a	a = erythema at edges of application
72 hr	2 2 2	0 0 0	a	
7 day	0 0 0	0 0 0	b	b = scaliness

Draize Score = 2.5

Draize Score = $[(\text{Erythema + Edema})_{24hr} + (\text{Erythema + Edema})_{72\,hr}] / [(2n)]$
where n = no. of animals

Statistics: No statistical analysis.

Conclusion

The primary skin irritation/corrosion study (4-hour semi-occlusive application) carried out with NEU 1161I (Canola Oil + Pyrethrins) in the rabbit resulted in a primary irritation index of 2.5 (moderately irritating) when applied to the intact rabbit skin. Although only 3 animals were used in this study, a quantitative assessment resulted; no meaningful additional information would be

gained from repeating this test with a greater number of test animals. The Toxicity Category is III (moderately irritating). This submission satisfies the data requirements for 152-14.

CONFIDENTIALITY AND GOOD LABORATORY PRACTICES STATEMENTS

A signed statement of no data confidentiality claims is made for the information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1) (A), (B), or (C).

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